NOTES

[GANN, 57, 427-429; August, 1966]

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POSSIBLE TRANSMISSION OF LEUKEMIA VIRUS IN AKR MICE THROUGH MILK

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No one doubts the viral etiology of spontaneous leukemia in AKR strain of mice. Gross5) postulated that in AKR and C58 mice leukemia virus is transmitted vertically from generation to generation through the embryo, most probably directly through the germinal cells. Studies with mice foster-nursed by high-leukemic mothers1,13) or inoculated with fresh milk of AKR mice6) did not cause an increase in leukemia incidence, in mice of low-leukemic strains. Recent studies reported, however, that highly potent leukemogenic viruses such as Passage A virus,7) Moloney's,8,11) and Graf-fi's,9) were transmitted to non-infected offspring through the milk of infected mothers. Electron microscopic studies revealed the presence of leukemia virus in the mammary gland of infected mothers.3) Although the presence of virus particles with morphological characteristics of the leukemia agent in the milk of AKR and C58 was demonstrated,20) no biological evidence is available to date indicating transmission via milk of the virus naturally present in AKR mice. The present short communication will give data which indicate possible transmission of AKR virus to offspring via milk.

Lilly et al.12) reported that the susceptibility of inbred mice to the induction of leukemia by the Gross virus is strongly influenced by the major histocompatibility gene H–2; mice which are homozygous for H–2k being highly susceptible, while mice lacking H–2k or heterozygous for H–2k being considerably less susceptible. Therefore, the F1 generation of mice, which are homozygous for H–2k, were used, obtained by crossing either females of the AKR(H–2k) strain and males of the C3Hf(H–2k):(AKR×C3Hf)F1, or females of the C3Hf and males of the AKR: (C3Hf×AKR)F1. The incidence of leukemia in our colony of AKR mice is approximately 80% with an average latency of 9.0 months,14) and that of C3Hf is extremely low (less than 1%) within a year after birth.

The F1 mice produced by C3Hf females and AKR males were divided into two groups; one group was nursed by their own mothers (C3Hf) and the other group by high-leukemic AKR mothers. In the latter group, all members of the litter were removed from C3Hf mothers within 24 hours (mostly less than 16 hours) after birth and immediately foster-nursed by
AKR mothers. All the females of the AKR strain used for foster-nursing were less than 4 months old and none of them developed leukemia during lactation or soon after weaning. All the experimental mice were weaned at the 30th day after birth and were allowed to live indefinitely until they died naturally or they were killed when they developed tumors or became moribund. All the survivors were killed at 360 days of age. All the animals were autopsied and different organs were dissected free for histological examination. Only mice surviving beyond the age of 153 days, the shortest latent period for the leukemia development, were included in the tabulation. Some leukemias found at the time of autopsy were transplanted subcutaneously into mice of the AKR and (C3Hf × AKR)F₁.

The incidence of leukemia and other tumors is shown in Table I. It is apparent from this table that the total incidence of leukemia (lymphoma and myeloid leukemia) in the F₁ mice from the AKR mothers (64.7% in the female and 44.2% in the male), which was almost the same level of the (C3HF × AKRF₁)F₁ hybrid mice foster-milked by AKR females.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Sex</th>
<th>No. of litters</th>
<th>No. of mice*</th>
<th>Lymphoma Av. age at lymphoma development (days)</th>
<th>Myeloid leukemia Av. age at leukemia development (days)</th>
<th>Other tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(AKR × C3HF)F₁</td>
<td>F</td>
<td>5</td>
<td>17</td>
<td>11 (64.7)</td>
<td>0 (0)</td>
<td>1 parotid tumor</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>4</td>
<td>18</td>
<td>8 (44.2)</td>
<td>0 (0)</td>
<td>1 parotid tumor</td>
</tr>
<tr>
<td>(C3HF × AKR)F₁</td>
<td>F</td>
<td>10</td>
<td>28</td>
<td>5 (17.9)</td>
<td>2 (7.1)</td>
<td>312.0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>10</td>
<td>23</td>
<td>3 (13.0)</td>
<td>2 (8.7)</td>
<td>345.5</td>
</tr>
<tr>
<td>(C3HF × AKR)F₁ foster-nursed by AKR females</td>
<td>F</td>
<td>10</td>
<td>23</td>
<td>12 (52.2)</td>
<td>2 (8.7)</td>
<td>330.0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>9</td>
<td>24</td>
<td>7 (29.2)</td>
<td>2 (8.3)</td>
<td>332.0</td>
</tr>
</tbody>
</table>

* Number of mice surviving beyond the age of 153 days, the shortest latent period for the leukemia development.
AKR hosts. The other 14 cases of leukemia grew only in the F1 animals.

It is known that in crosses between high- and low-leukemia strains of mice, F1 hybrids from high-leukemic mothers usually show a higher incidence of leukemia than F1 hybrids from low-leukemic mothers. Foster-nursing by females of certain low-leukemia strains, but not of other strains, significantly lowered the incidence of leukemia in high-leukemia strains. This effect was attributed to the maternal resistance factor present in the milk of some of low-leukemic mothers. The nature of this factor, however, remains unclarified. Although the present study could not rule out the presence of this factor, it strongly suggests the possibility that in AKR mice, leukemia virus is transmitted from normal mother to offspring through the mother's milk.

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References